

# (12) United States Patent

## Shin et al.

#### US 10,465,241 B2 (10) Patent No.:

(45) Date of Patent: Nov. 5, 2019

### (54) HIGH RESOLUTION STR ANALYSIS USING NEXT GENERATION SEQUENCING

(71) Applicant: The Board of Trustees of the Leland Stanford Junior University, Stanford,

CA (US)

(72) Inventors: Giwon Shin, Stanford, CA (US); Billy

Tsz Cheong Lau, Palo Alto, CA (US); HoJoon Lee, Stanford, CA (US): Hanlee P. Ji, Stanford, CA (US)

(73) Assignee: THE BOARD OF TRUSTEES OF

THE LELEAND STANFORD JUNIOR UNIVERSITY, Stanford, CA

(US)

(\*) Notice: Subject to any disclaimer, the term of this

patent is extended or adjusted under 35

U.S.C. 154(b) by 639 days.

Appl. No.: 15/177,115

(22)Filed: Jun. 8, 2016

(65)**Prior Publication Data** 

> US 2016/0362751 A1 Dec. 15, 2016

### Related U.S. Application Data

- Provisional application No. 62/175,985, filed on Jun. 15, 2015, provisional application No. 62/200,904, filed on Aug. 4, 2015.
- (51) Int. Cl. C120 1/6869 (2018.01)

U.S. Cl. 

Field of Classification Search

See application file for complete search history.

#### (56)References Cited

#### **PUBLICATIONS**

Anvar, et al. "TSSV: a tool for characterization of complex allelic variants in pure and mixed genomes", vol. 30 No. 12 2014, pp.

Bornman, et al. "Short-read, high-throughput sequencing technology for STR genotyping", Biotech Rapid Dispatches.; 2012: 1-6. Cao, et al "Inferring short tandem repeat variation from paired-end short reads", Nucleic Acids Research, 2014, vol. 42, No. 3, e16, pp.

Carlson, et al. "MIPSTR: a method for multiplex genotyping of germline and somatic STR variation across many individuals", Genome Research, 2015, 25:750-761.

(Continued)

Primary Examiner — Kaijiang Zhang (74) Attorney, Agent, or Firm — James S. Keddie; Bozicevic, Field & Francis LLP

#### ABSTRACT (57)

A method for analyzing short tandem repeats (STRs) is described herein. In some embodiments, the method comprises: separately digesting two portions of a genomic sample at sites that are upstream and downstream of an STR; fragmenting those products; ligating adaptors to the fragmentation products; selectively amplifying part of the top strand but not the bottom strand of the ligation products derived from the first portion, and part of the bottom strand but not the top strand of the ligation products derived from the second portion; sequencing at least some of the amplification products to produce a plurality of top strand reads and a plurality of bottom strand reads; and counting the number of STR repeats in a sequence read. A kit for performing the method is also provided.

## 16 Claims, 20 Drawing Sheets Specification includes a Sequence Listing.

